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Generic and biosimilar medicines: quid?

EDITORIAL

Steven Simoens [1]
[1] Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Belgium

INTRODUCTION

Once intellectual property protection, data and marketing exclusivity of reference medicines have expired, generic medicines and biosimilar medicines can enter the off-patent market. This market entry is conditional on the approval of marketing authorization, pricing and reimbursement. Given that there tends to be confusion surrounding generic and biosimilar medicines, this Editorial introduces basic concepts related to generic and biosimilar medicines and presents the different studies and articles included in this supplement dedicated to generic and biosimilar medicines.

GENERIC MEDICINES

A generic medicine is a medicinal product which has the same qualitative and quantitative composition in active substances as the reference chemical medicine; has the same strength, pharmaceutical form and administration route as the reference chemical medicine; and has the same bio-availability as the reference chemical medicine as demonstrated by appropriate bio-availability studies [1].

There has been controversy over whether differences in bio-availability that fall within the variation allowed by medicines agencies can lead to a different safety and efficacy profile between the generic medicine and the reference medicine. This controversy does not relate to the majority of small molecule medicines, where the generic medicine has the same quality, safety and efficacy as the reference medicine and, therefore, the generic and reference medicines are interchangeable. The question of bio-equivalence tends to be asked with respect to narrow therapeutic index medicines (e.g. anti-epileptic medicines), where the difference between the effective dose and the toxic dose is small. Concerns about bio-equivalence in narrow therapeutic index medicines seems to be unwarranted as multiple literature reviews have supported the clinical equivalence of generic and reference versions of narrow therapeutic index medicines [2,3]. If differences in health outcomes are observed between such generic and reference medicines, recent evidence suggests that this does not result from issues surrounding bio-equivalence, but from other factors such as undue concerns from patients or physicians about the effectiveness of generic medicines or the act itself of refilling a prescription [2,4].

Due to their lower costs of research and development (as there is for example no need to replicate pre-clinical tests and clinical trials), generic medicines tend to be less expensive than reference medicines. Vogler et al. [5] calculated the difference in ex-factory prices between five generic and reference medicines for 16 European countries in November 2011. These authors found that price differences between generic and reference medicines were limited or non-existent for some countries, but varied between 50% and approximately 100% for other countries. Larger price differences between generic and reference medicines and lower generic medicine prices tended to be observed in countries that had implemented effective generic medicine policies based on competition and enforcement (such as mandatory generic substitution and/or prescribing by international non-proprietary name).

As a result of their lower price, generic medicines play a crucial role in sustaining patient access to health care. Generic medicines are today used in the treatment of acute as well as chronic diseases such as asthma, bacterial infections, cancer, diabetes, depression, epilepsy, gastro-intestinal and inflammatory disorders, osteoporosis, pain, Parkinson's disease and rheumatoid arthritis. The availability of generic medicines not only improves the cost-effectiveness of existing pharmacotherapy, but may also make it cost-effective to manage previously untreated patients.

Therefore, Godman et al. [6] explored the contribution that low-priced generic medicines can make to enhance prescribing efficiency and support comprehensive and equitable health care. This review of the European experience showed that the implementation of various supply-side measures (i.e. measures related to market access, (refe-

Corresponding authors
Dr. Steven Simoens
Department of Pharmaceutical and Pharmacological Sciences, KU Leuven
Onderwijs en Navorsing 2, Herestraat 49, P.O. Box 521, 3000 Leuven, Belgium
Tel: +32-(0)16-323465
Fax: +32-(0)16-323468
steven.simoens@pharm.kuleuven.be

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rence) pricing and reimbursement of generic medicines) and demand-side measures (i.e. incentives for physicians, pharmacists and patients to use generic medicines) has reduced generic medicine prices and supported their utilization. This has allowed countries to save resources without compromising the quality, safety and efficacy of care.

However, market access of generic medicines in Europe is inhibited or delayed by the decline in true innovation in the pharmaceutical sector; shortcomings in current procedures governing intellectual property protection (e.g. patent linkage, evergreening tactics), data and marketing exclusivity, and marketing authorization; pricing and reimbursement delays for generic medicines. There is a need to prevent evergreening tactics; to delink intellectual property protection issues from marketing authorization, pricing and reimbursement procedures; and to speed up pricing and reimbursement decisions for generic medicines [7].

BIOSIMILAR MEDICINES

In the case of biological medicines, a biosimilar medicine can enter the off-patent market which is similar, but not identical to the reference medicine. In the European Union, marketing authorization of biosimilar medicines is granted by considering non-clinical studies, comparative quality and pharmacokinetic studies, pharmacodynamic studies, toxicology studies, comparative clinical efficacy and tolerability studies [8].

The expiry of intellectual property protection, data and marketing exclusivity on biological medicines will not only open the door to the development of biosimilar medicines, but will also enable the traditional generic medicines industry to move from a 'copy-cat' business model to an innovative business model that relies on investment in research and development, and on the creation of expertise in biological development and manufacturing. Based on qualitative research, Barei et al. [9] showed that the switch from generic to biosimilar medicines appears to be driven by the lack of innovation in product portfolios, price pressure, competition and industrial evolution. At the same time, the development of biosimilar medicines is a source of innovation in itself as it requires the application of new technical, scientific, economic and commercial competencies. In this way, biosimilar medicines can provide a significant societal contribution by means of cost reduction and improved access to high-quality, innovative pharmacotherapy.

REFERENCES

1. European Commission. Directive 2004/27/EC of the European Parliament and of the Council of 31st March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use. *Off J EU* 2004; 30th April: 34-57
2. Kesselheim AS, Stedman MR, Bubrick EJ, et al. Seizure outcomes following the use of generic versus brand-name antiepileptic drugs: a systematic review and meta-analysis. *Drugs* 2010; 70: 605-21; http://dx.doi.org/10.2165/10898530-000000000-00000
3. Kesselheim AS, Misono AS, Lee JL, et al. Clinical equivalence of generic and brand-name drugs used in cardiovascular disease: a systematic review and meta-analysis. *JAMA* 2008; 300: 2514-26; http://dx.doi.org/10.1001/jama.2008.758
4. Gagne JJ, Avorn J, Shrank WH, et al. Refilling and switching of antiepileptic drugs and seizure-related events. *Clin Pharmacol Ther* 2010; 88: 347-53; http://dx.doi.org/10.1038/clpt.2010.90
5. Vogler S. How large are the differences between originator and generic prices? Analysis of five molecules in 16 European countries. *Farmeconomia* 2012; 13 (Suppl. 3): 29-41
6. Godman B, Bennie M, Baumgärtel C, et al. Essential to increase the use of generics in Europe to maintain comprehensive healthcare? *Farmeconomia* 2012; 13 (Suppl. 3): 5-20
7. Dylst P, Vulto A, Simoens S. Overcoming challenges in market access of generic medicines in the European Union. *J Generic Med* 2012; 9: 21-8; http://dx.doi.org/10.1177/1741134312441107
8. Declerck PJ, Simoens S. A European perspective on the market accessibility of biosimilars. *Biosimilars* 2012; 2: 33-40
9. Barei F, Le Pen C, Simoens S. From generic to biosimilar drugs: why take an innovative pace? *Farmeconomia* 2012; 13 (Suppl. 3): 21-27